

Prostatic Hyperplasia & Cancer Prostate

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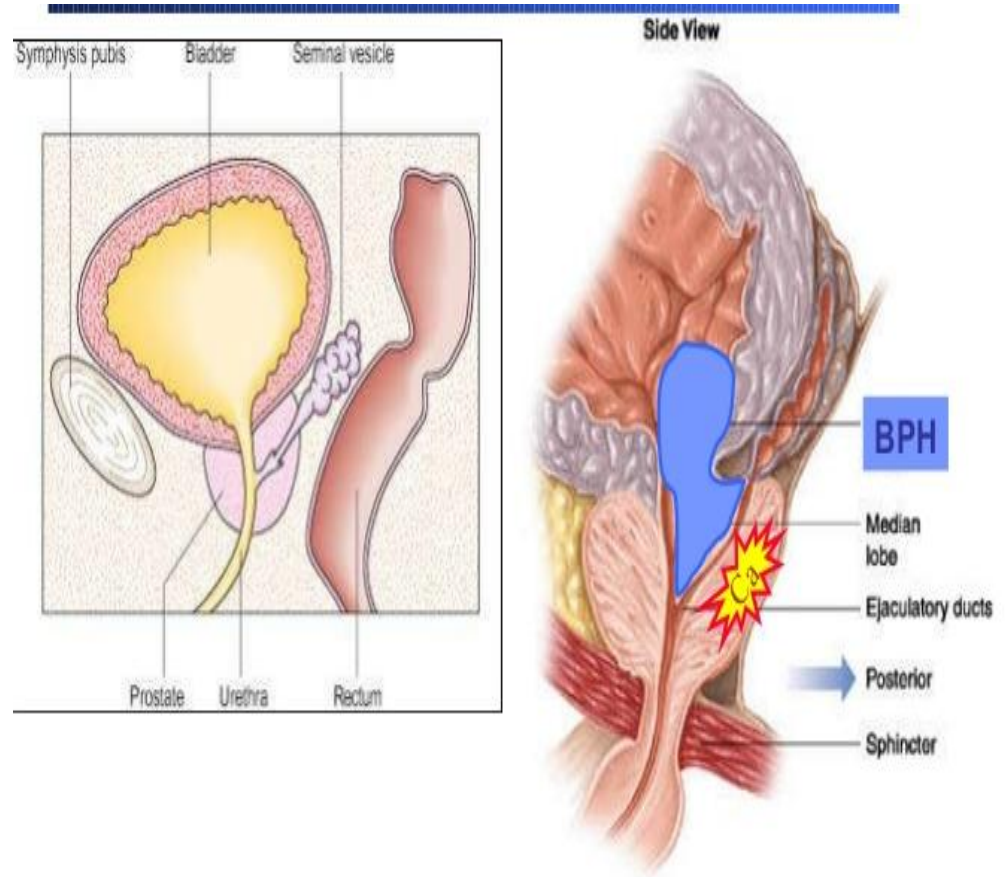
Objectives

By the end of this lecture the students must be able to :

- Discuss benign prostatic hyperplasia, it's pathological feature & clinical finding.
- Discuss Cancer Prostate , it's etiology, pathological feature, clinical finding, spread & Gleason system grading .

Anatomy of the prostate

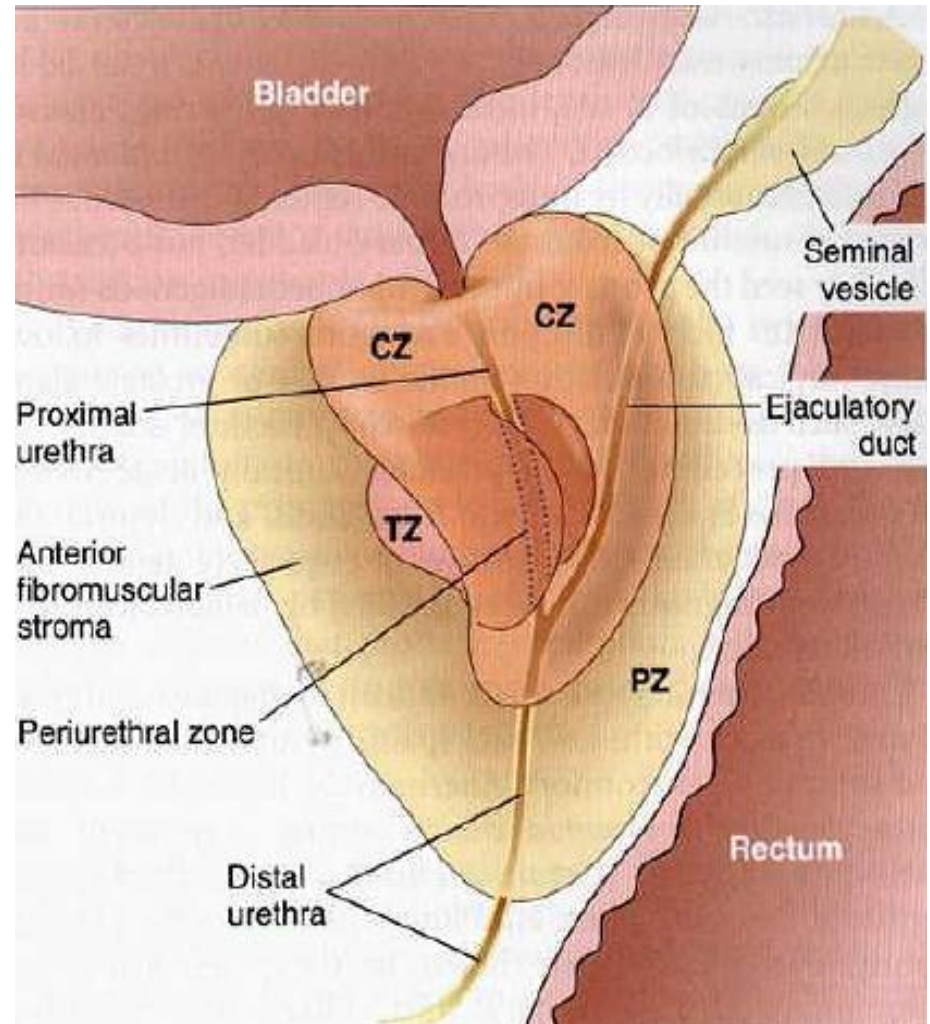
- Retroperitoneal organ encircling the neck of the urinary bladder & urethra
- Devoid of a distinct capsule
- In normal adult, weighs approximately 20g
- Can be divided into 4 biologically & anatomically distinct zones or regions



Zones of the prostate

- Peripheral
- Central
- Transitional
- Region of the anterior fibromuscular stroma

Most hyperplasias arise in the transitional zones, whereas most carcinomas arise in the peripheral zone.



Histology of the prostate

- **Tubuloalveolar organ** composed of glands which are lined by epithelium
- Lining is composed of 2 layers of cells: **a basal layer of low cuboidal epithelium covered by a layer of columnar secretory cells**
- The epithelium shows papillary infolding & rests on a basement membrane
- Glands are separated by abundant **fibromuscular stroma**

Normal Histology: Fibro-Muscular-Gland

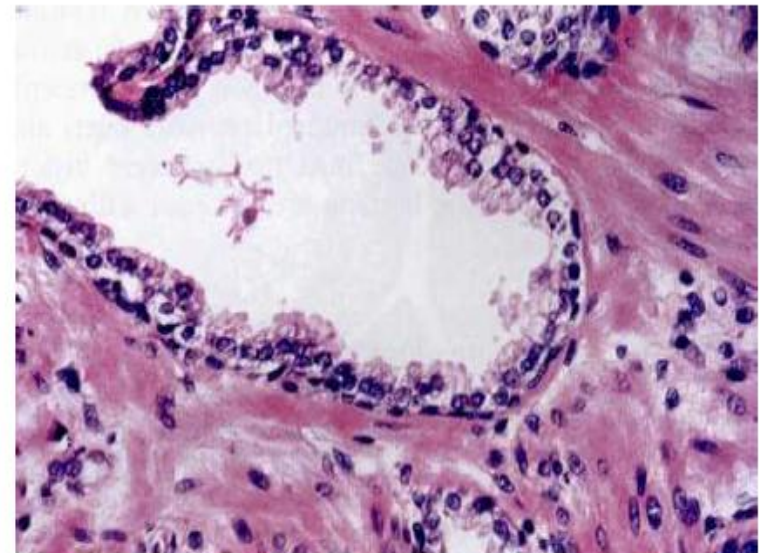
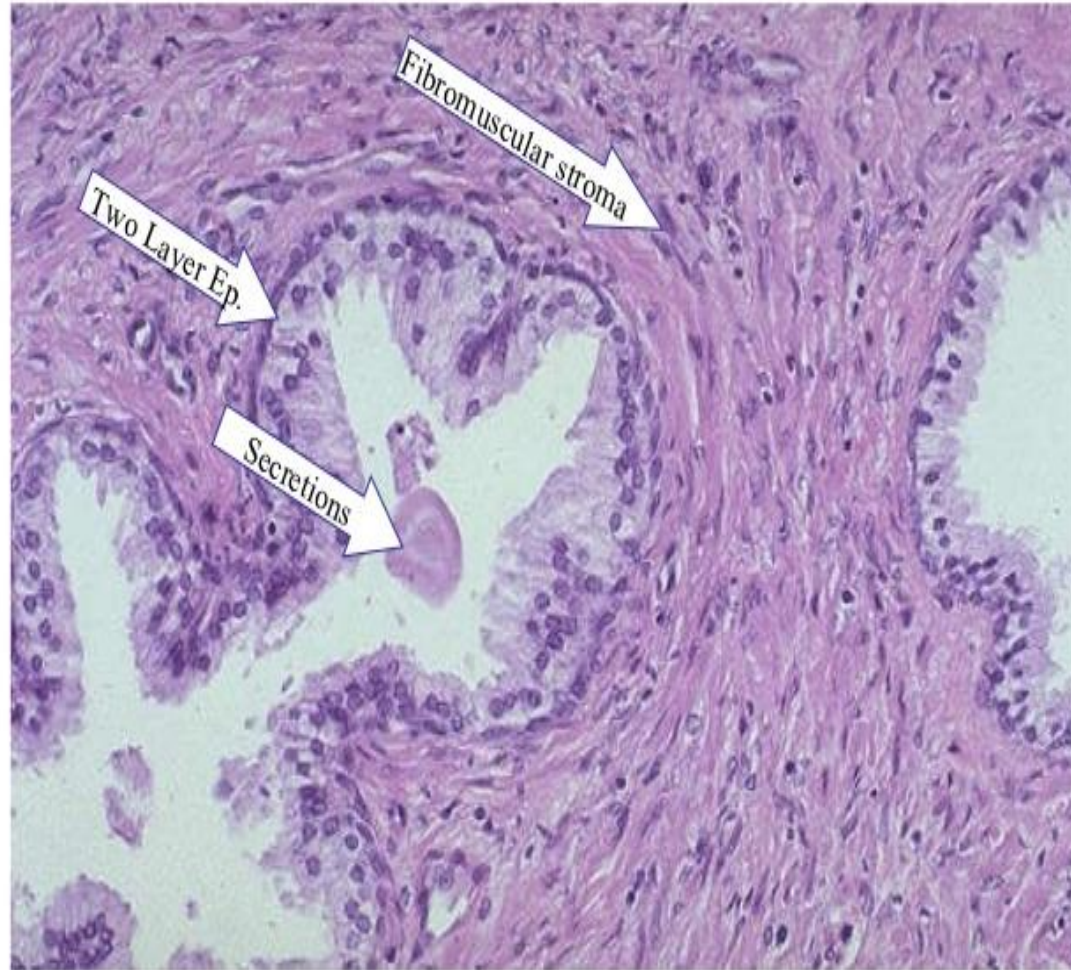


FIGURE 21—31 Benign prostate gland with basal cell and secretory cell layer.

Enlargement of Prostate:

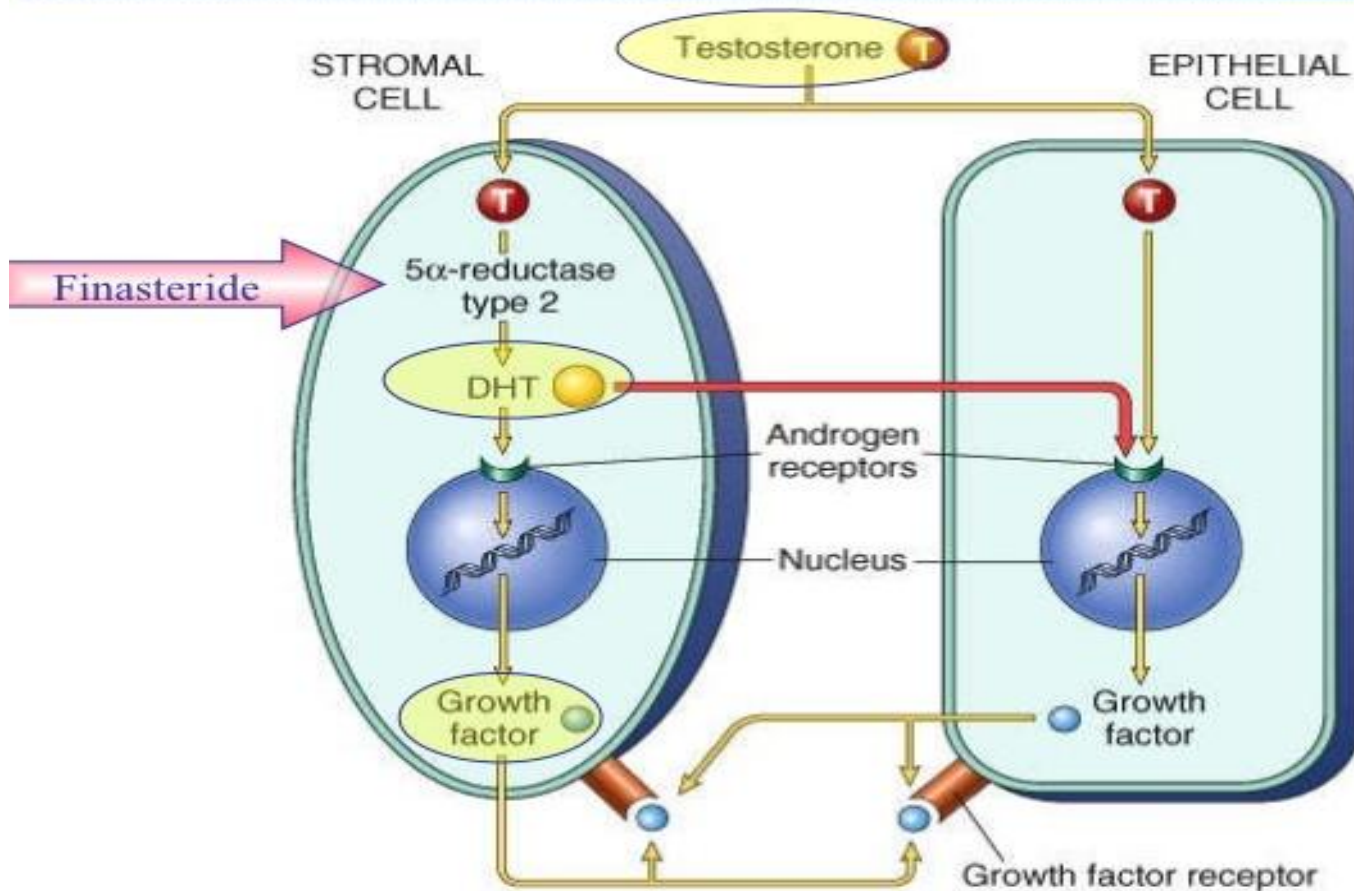
- Inflammations – infections
- BPH – Benign Prostatic Hyperplasia
- Neoplasms – Carcinoma.

Disease	Incidence	location	Morph -DRE	SAP
BPH	>80% at 80y	Central / periurethra	Nodular Hyperplasia, Firm, smooth Median groove	normal
Carcinoma	Latent is Common. Clinical not.	Posterior subcapsular	Adenocarcinoma Hard stony, irregular, fixed No median groove.	Raised.

Nodular hyperplasia/Benign prostatic hyperplasia (BPH)

- Common non-neoplastic hormone induced hyperplasia.
- 75% among men aged 70-80years
- Over 90% in people aged over 90y
- Involves peri urethral & central zones.
- Rare before the age of 40y.
- Hormone induced – Androgens.

Patho-Physiology: Testosterone $\rightarrow$ DHT $\rightarrow$ GF



Simplified scheme of the pathogenesis of prostatic hyperplasia. The central role of the stromal cells in generating dihydrotestosterone, (DHT) should be noted

Pathologic features of BPH:

Gross:

- Prostate enlarged, nodular, firm & rubbery
- Weight: 2x or more than normal
- Central portion expanded by nodules that compress the peripheral part of the prostate (forming a “surgical” or pseudocapsule)
- Urethra is compressed, deformed & tortuous



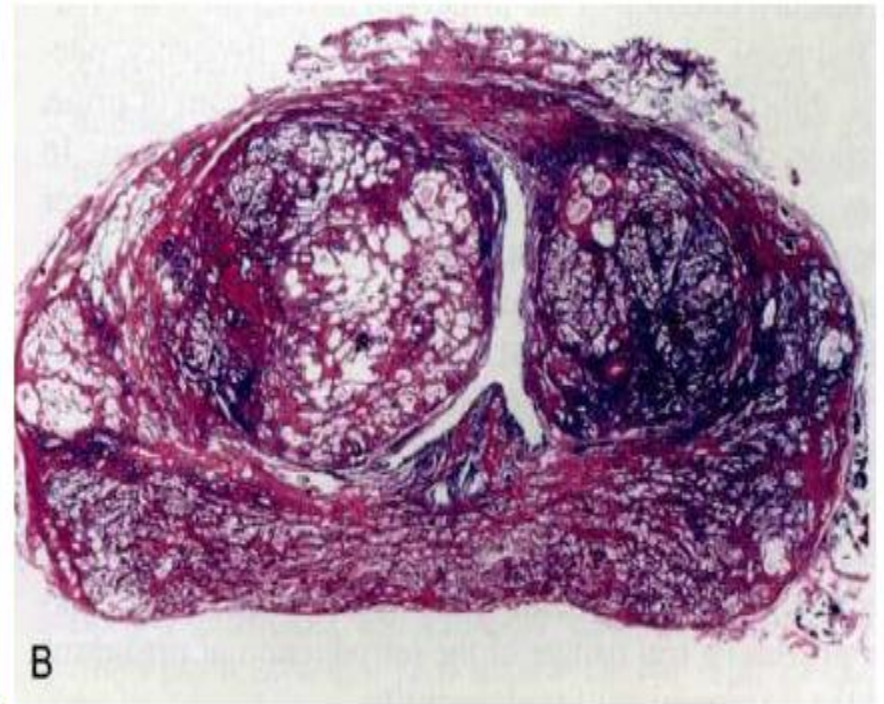
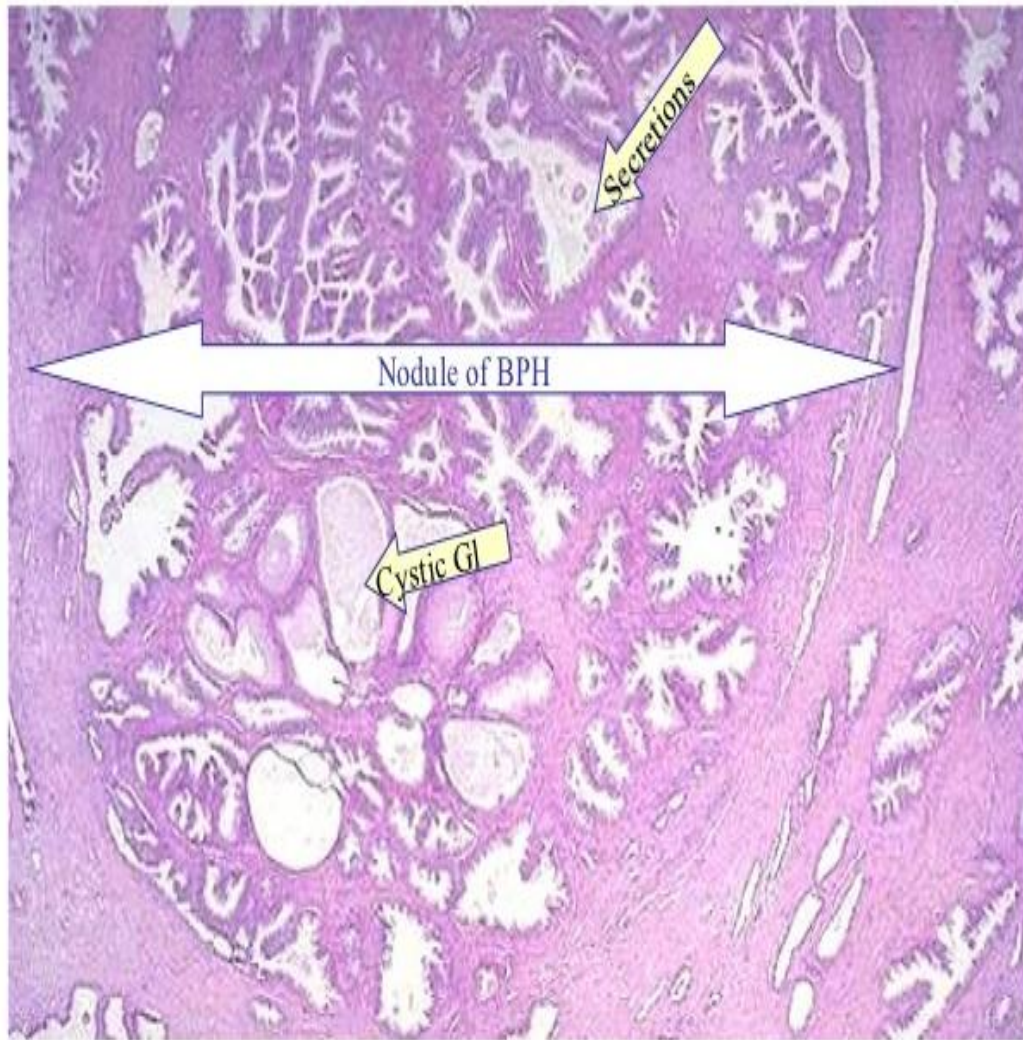


FIGURE 21-33 Nodular prostatic hyperplasia. A, Well-defined nodules of BPH compress the urethra into a slitlike lumen. B, A microscopic view of a whole mount of the prostate shows nodules of hyperplastic glands on both sides of the urethra.

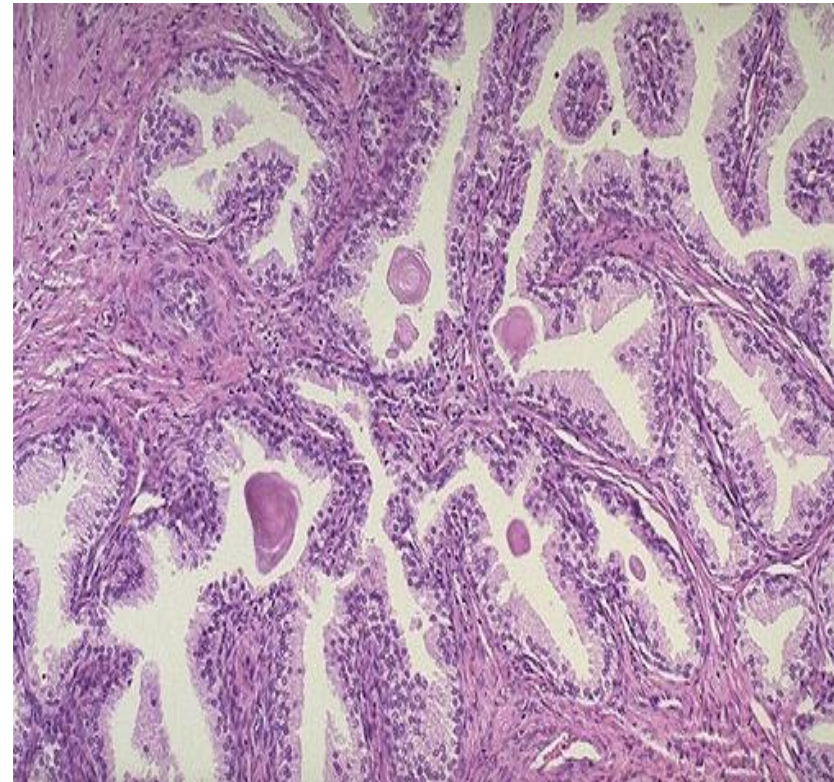
Microscopy of BPH

- **Nodular** prostatic **hyperplasia** consists of **nodules of glands and** intervening **stroma** (both).
- The glands variably sized, with larger glands have more prominent **papillary** infoldings, **double layered epithelium** (**like normal**) some may be **cystic** with secretions.
- Stroma is composed of hyperplastic smooth muscle cells & fibroblasts.
- Nodular hyperplasia is **NOT** a precursor to carcinoma.

BPH: Nodular, Gland+stromal hyperplasia



Benign prostatic hyperplasia involving both glands and stroma



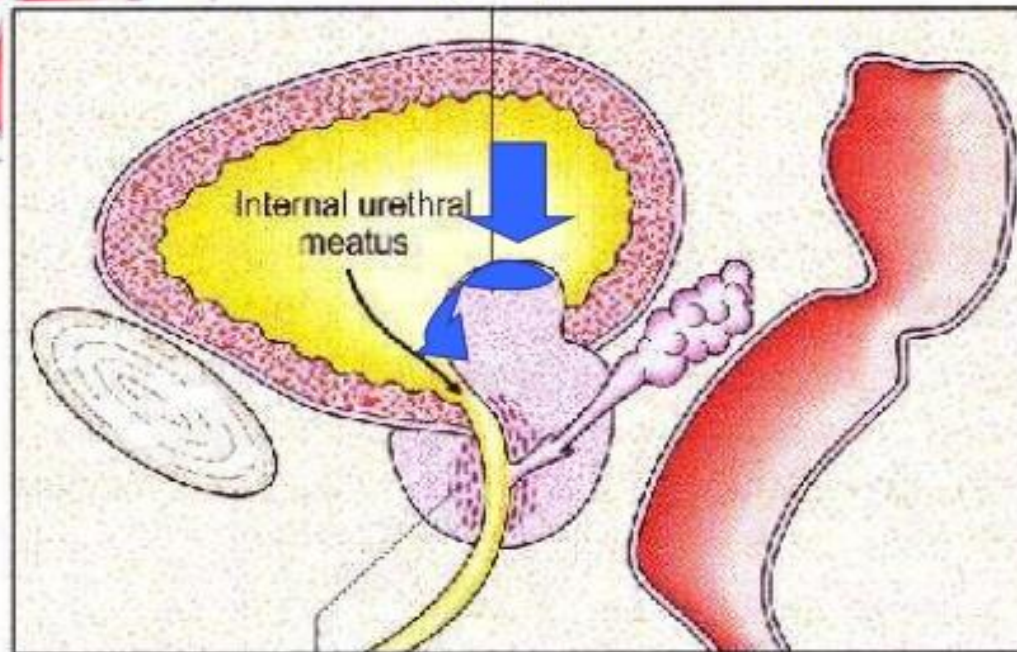
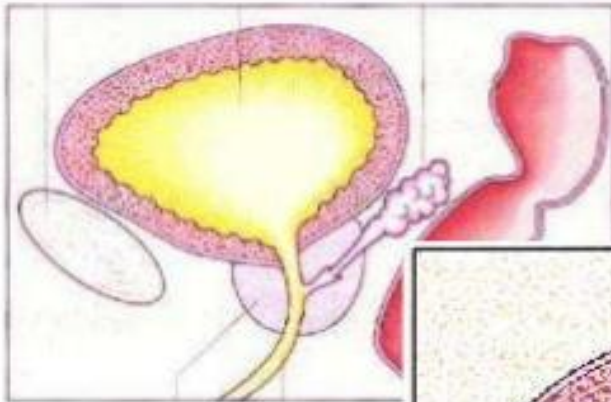
High power view of glandular hyperplasia

Clinical features of BPH

- **Dysuria** (urge to urinate frequently, weak stream, halting, incomplete emptying of the urinary bladder)
- Urinary bladder infections
- Acute urinary retention which requires immediate catheterization

BPH-mechanism of obstruction:

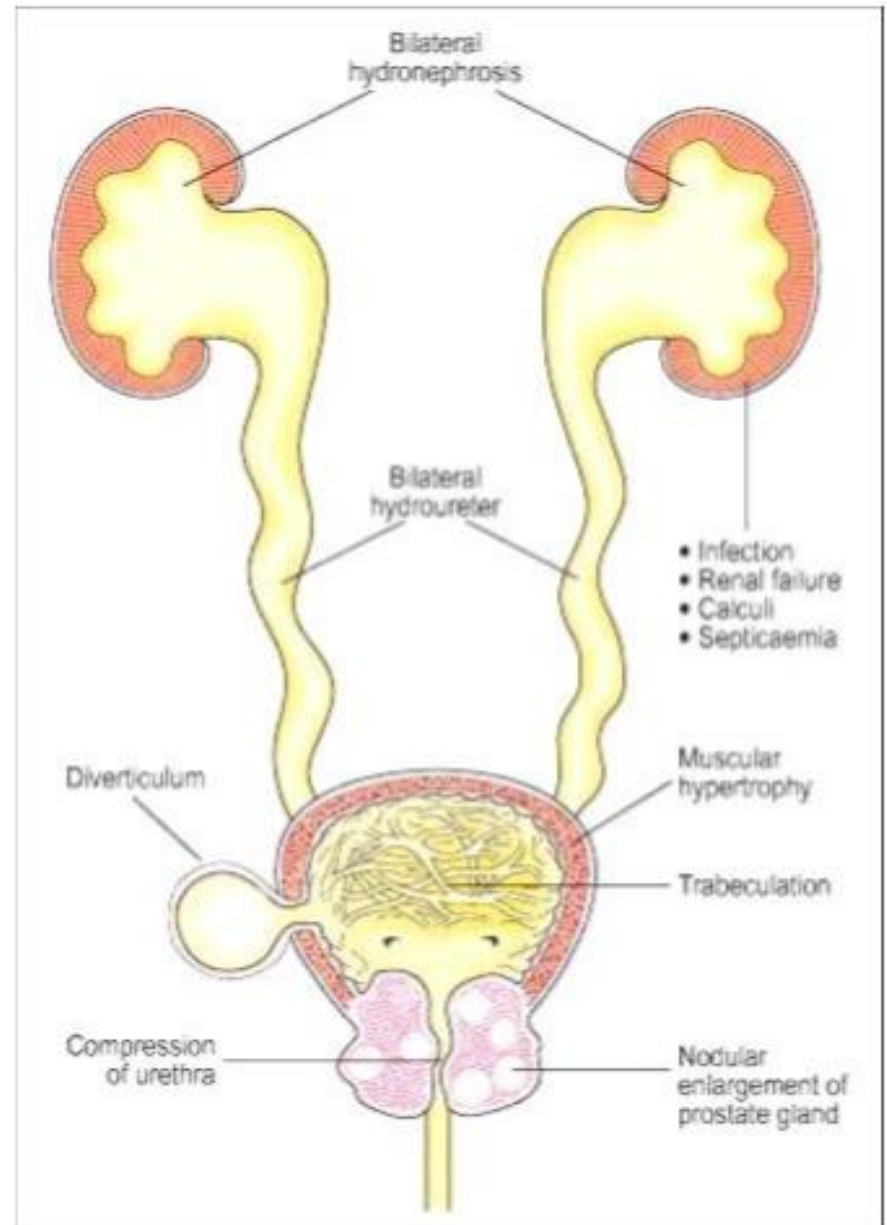
- Median lobe (3rd lobe)
- Ball valve mechanism
- Obstruction.
- Urgency/hesitation..



BPH-Complications:

1. Obstructive Uropathy
2. Bladder hypertrophy
3. Trabeculation
4. Diverticula formation
5. Hydroureter – bilateral
6. Hydronephrosis
7. Lithiasis / stone.
8. Secondary infection.

- Not a risk factor for Carcinoma prostate.



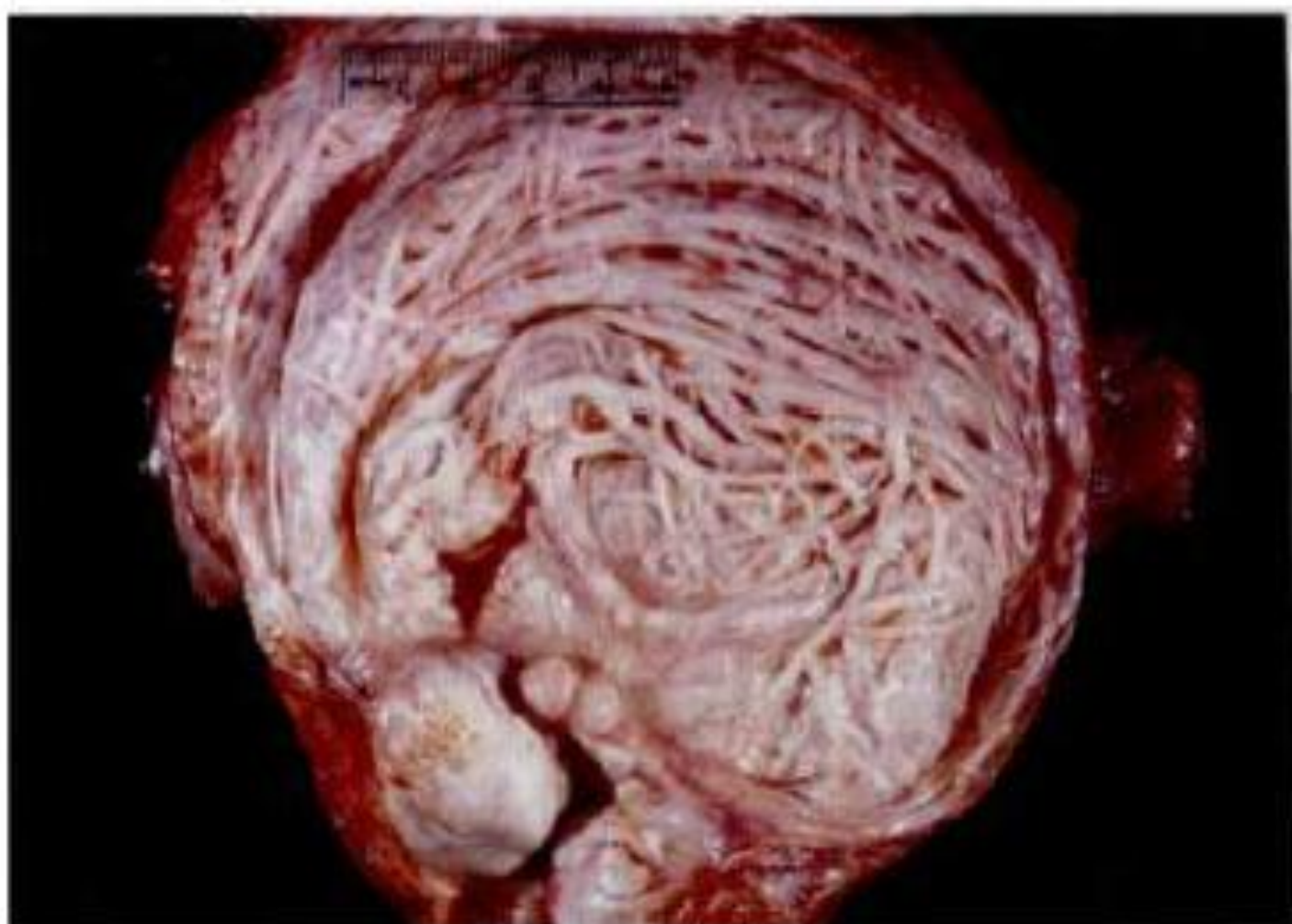


FIGURE 21—13 Hypertrophy and trabeculation of bladder wall secondary to polypoid hyperplasia of the prostate.

Prostatic carcinoma

Key facts:

- Disease of old age (**over 50 years**). Seen in over 70% of men over 70y old.
- Many of these carcinoma are small and clinically insignificant **.(Incident ca)**
- Role of hormones: Ca prostate never develops in men castrated before puberty.
- Prostate specific antigen **(PSA)** is used for **screening** & **monitoring of tumors**.
- PSA is **sensitive** but has **low specificity**.

Etiology

1. Endocrinologic factors- Androgens
2. Racial factors- More common in African Americans than in whites, Japanese or Chinese
3. Environmental factors- high fat diet, exposure to polycyclic aromatic hydrocarbons ??
4. Genetic basis- familial cases
5. Acquired somatic mutation (TMPRSS2-ETS fusion genes)
6. BPH- not proved

Prostatic intraepithelial neoplasia (PIN)

- A **precancerous** cellular proliferation found in a single acinus or small group of acini.
- Consists of benign glands with intra-acinar proliferation of cells that demonstrate nuclear **anaplasia**
- PIN glands are surrounded by a patchy layer of basal cells & a basement membrane

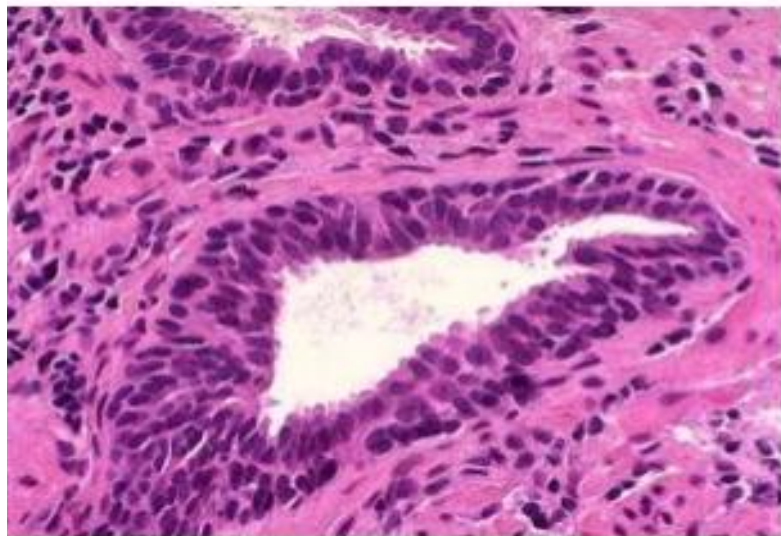
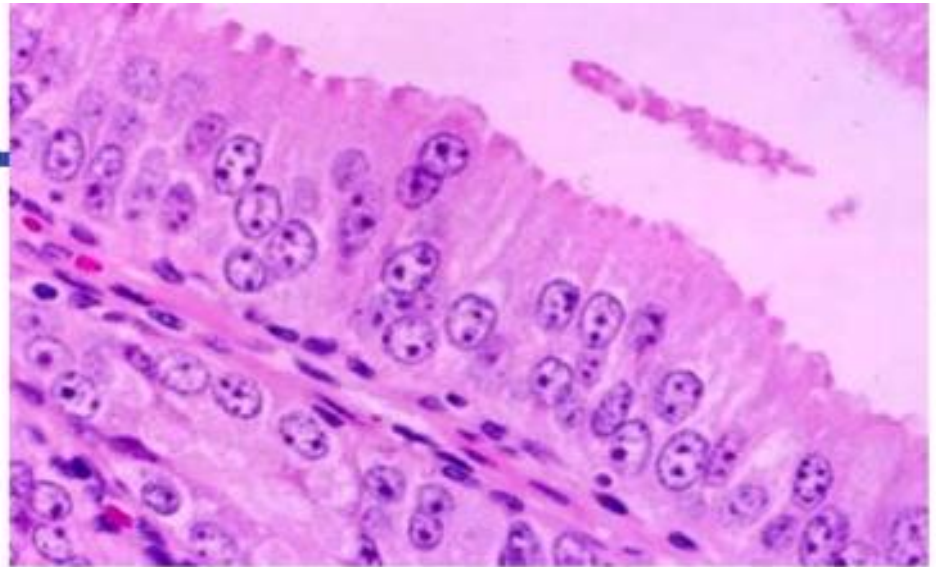
PIN:

Crowding, stratification

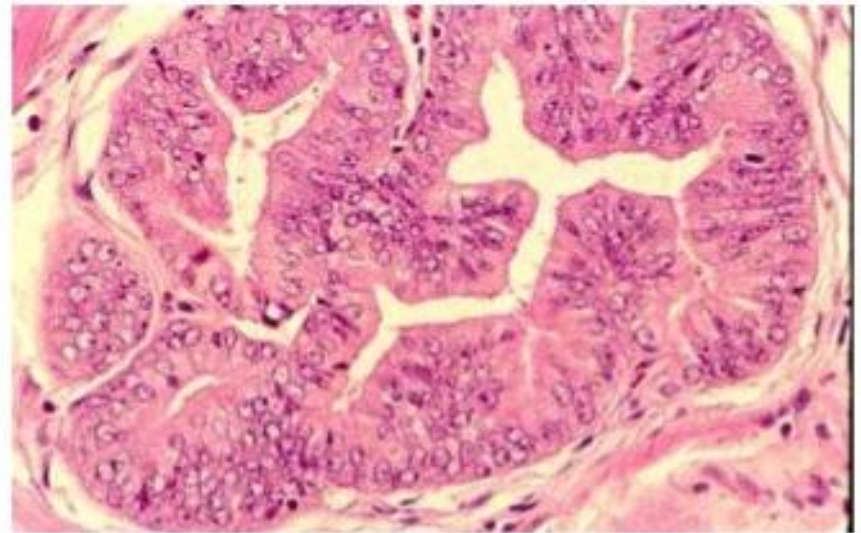
Pleomorphism

Nuclear enlargement.

Low grade PIN →



High grade PIN ↑



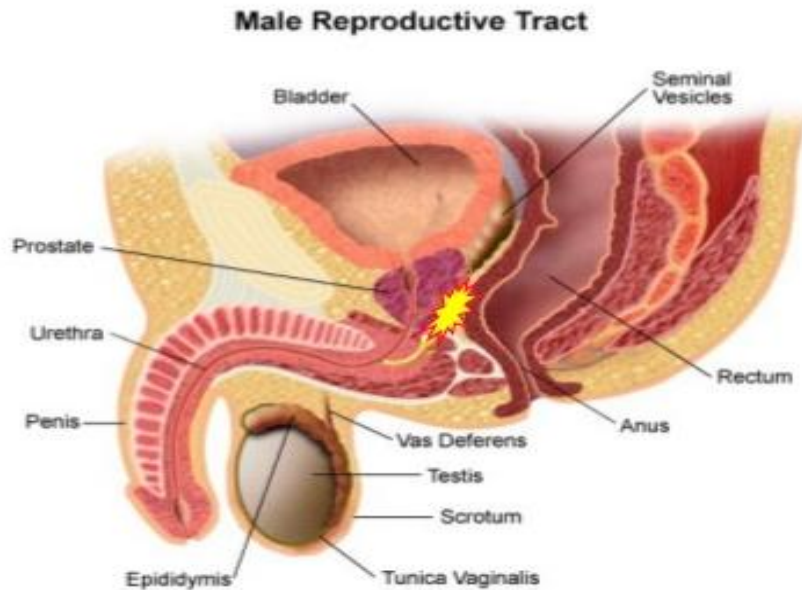
Grade II - III ↑

**The finding of PIN suggests that
prostatic adenocarcinoma may also
be present**

Symptoms

- By the time symptoms appear, the carcinoma, is palpable on PR as a hard mass which is fixed to surrounding tissue.
- Symptoms are:
 - Urinary obstruction with dysuria
 - Retention of urine
 - Hematuria
 - Bony pain due to metastases

Pathologic features of prostatic carcinoma



- Posterior Lateral lobes: Carcinoma
- Rectal examination.
- Solid, hard, adenocarcinoma

Multifocal induration, most often in the outer zones & **posterior lobe** (can be palpated on rectal examination)



Adeno Carcinoma + BPH



Adenocarcinoma of the prostate . Carcinomatous tissue is seen on the posterior aspect (lower cleft). Note the solid whiter tissue of cancer in contrast to the spongy appearance of the benign peripheral zone on the contralateral side.

Prostate Ad.Ca:

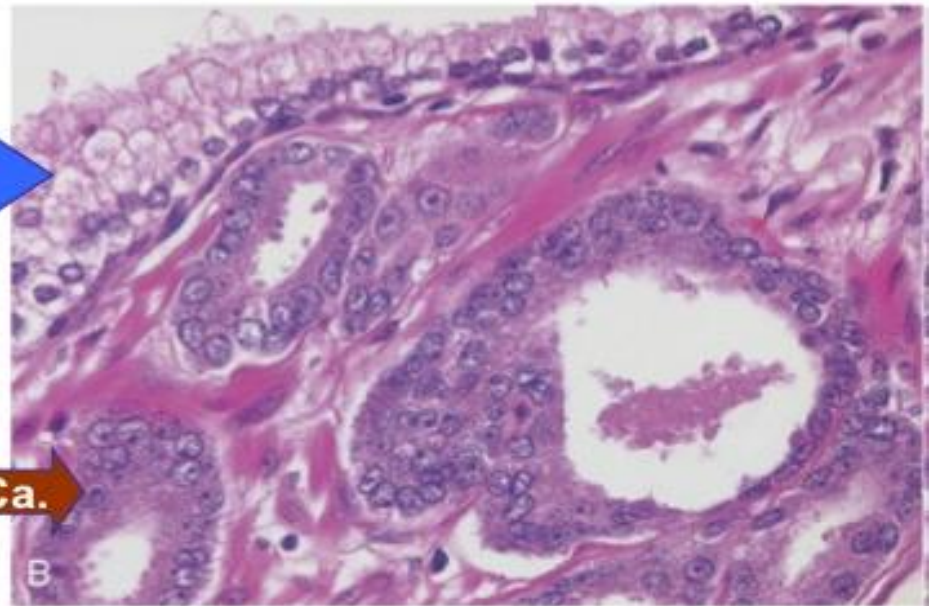
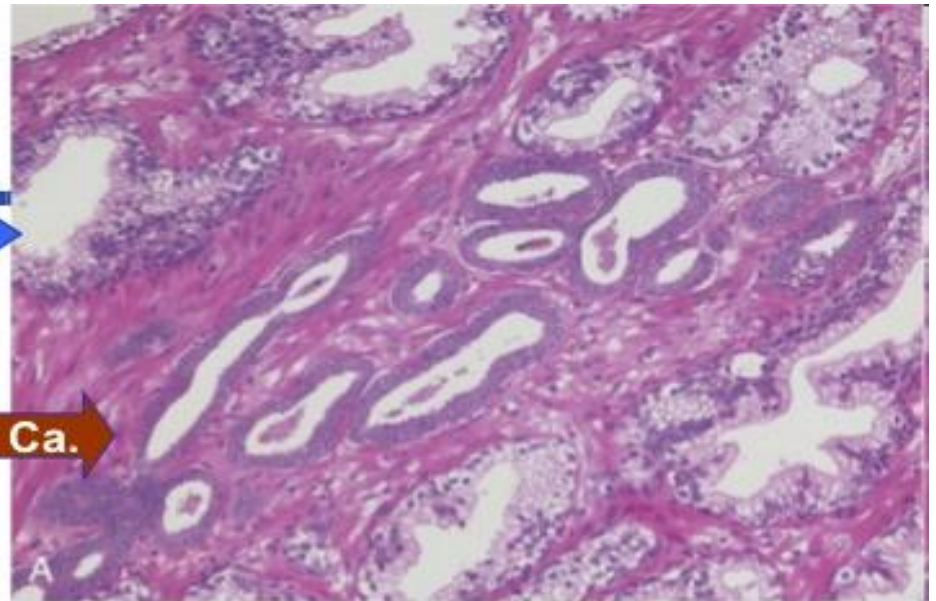
Normal

Benign:

- Double layer,
- Secretion (clear cytopl)
- Uniform cells
- Papillary folds

Malignant

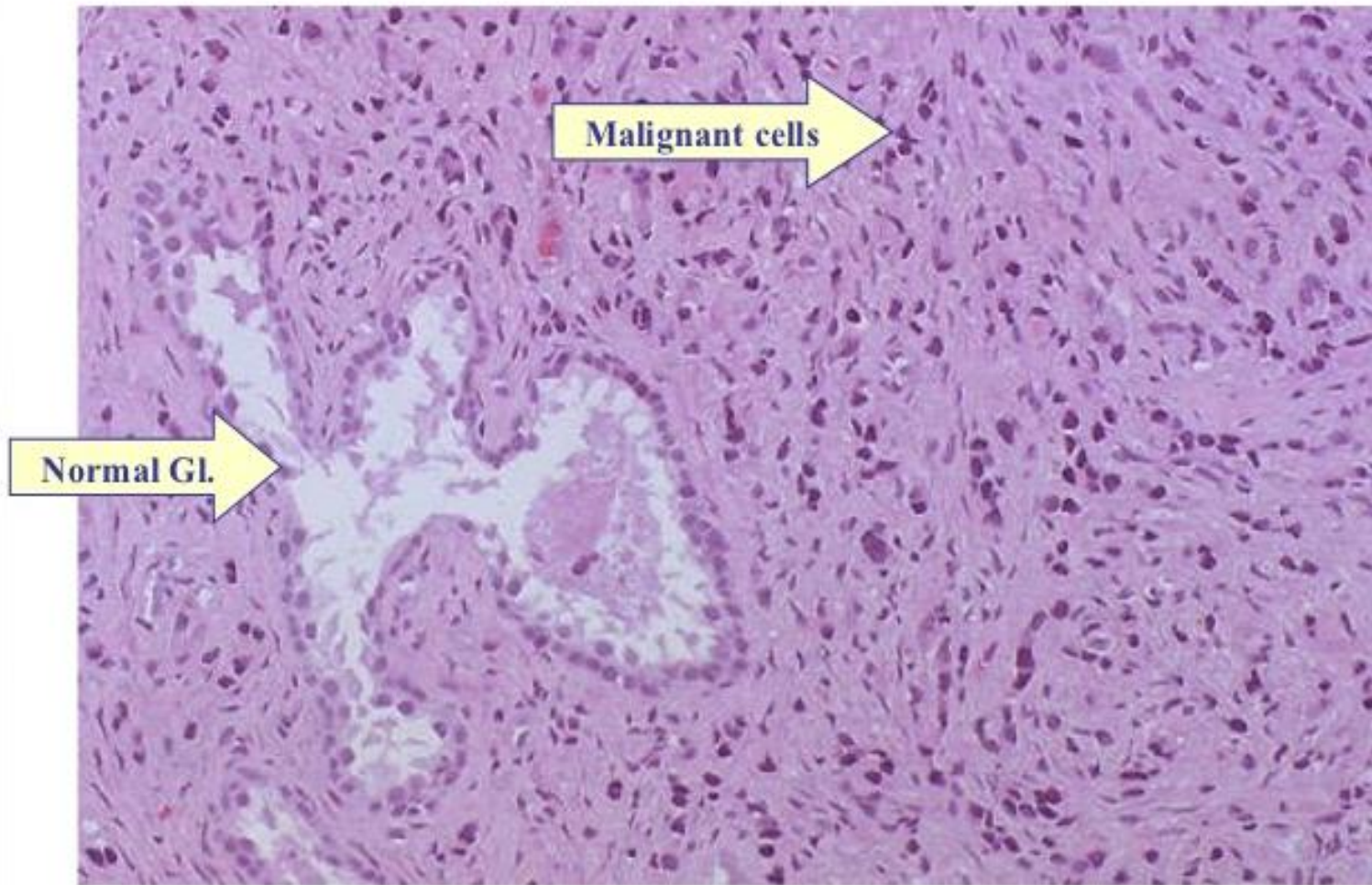
- Single / crowded.
- Less/no secretion.
- Uniform/Pleomorphic
- No papillary folds. But crowding & clustering.

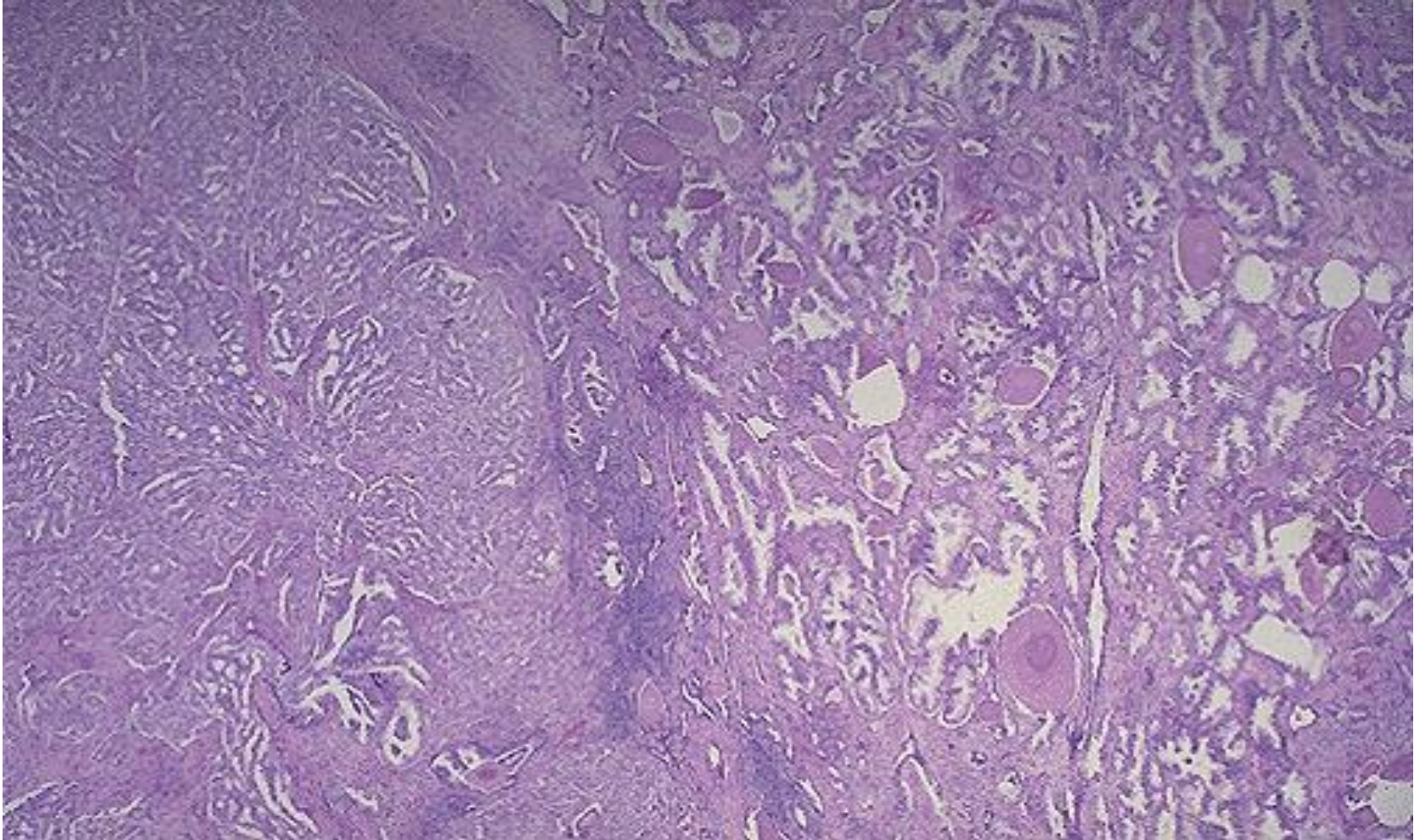


On histology, carcinoma prostate can be:

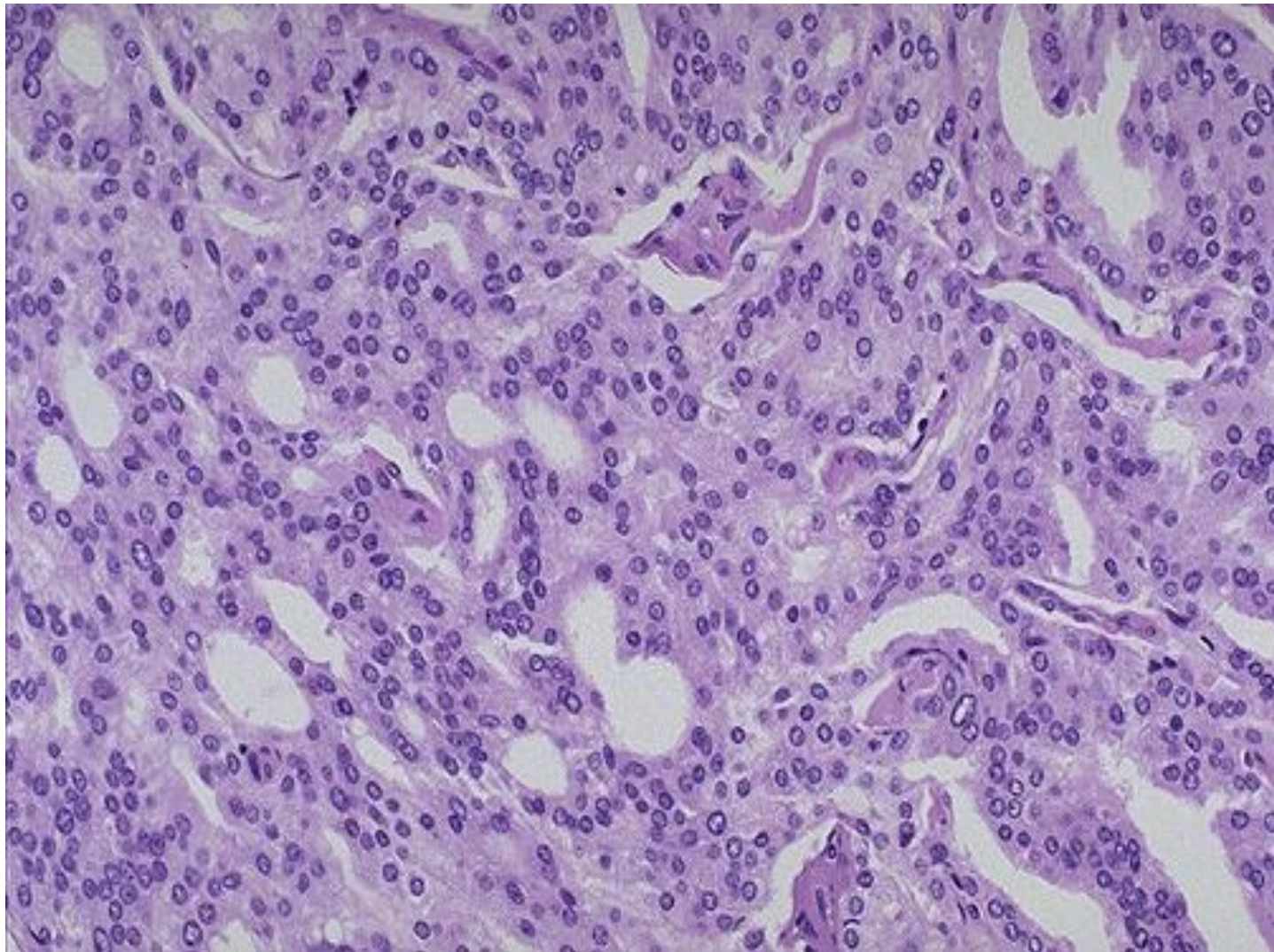
- Adenocarcinoma (96% of cases)
- Transitional cell carcinoma
- Squamous cell carcinoma
- Undifferentiated carcinoma

Prostate cancer poorly differentiated

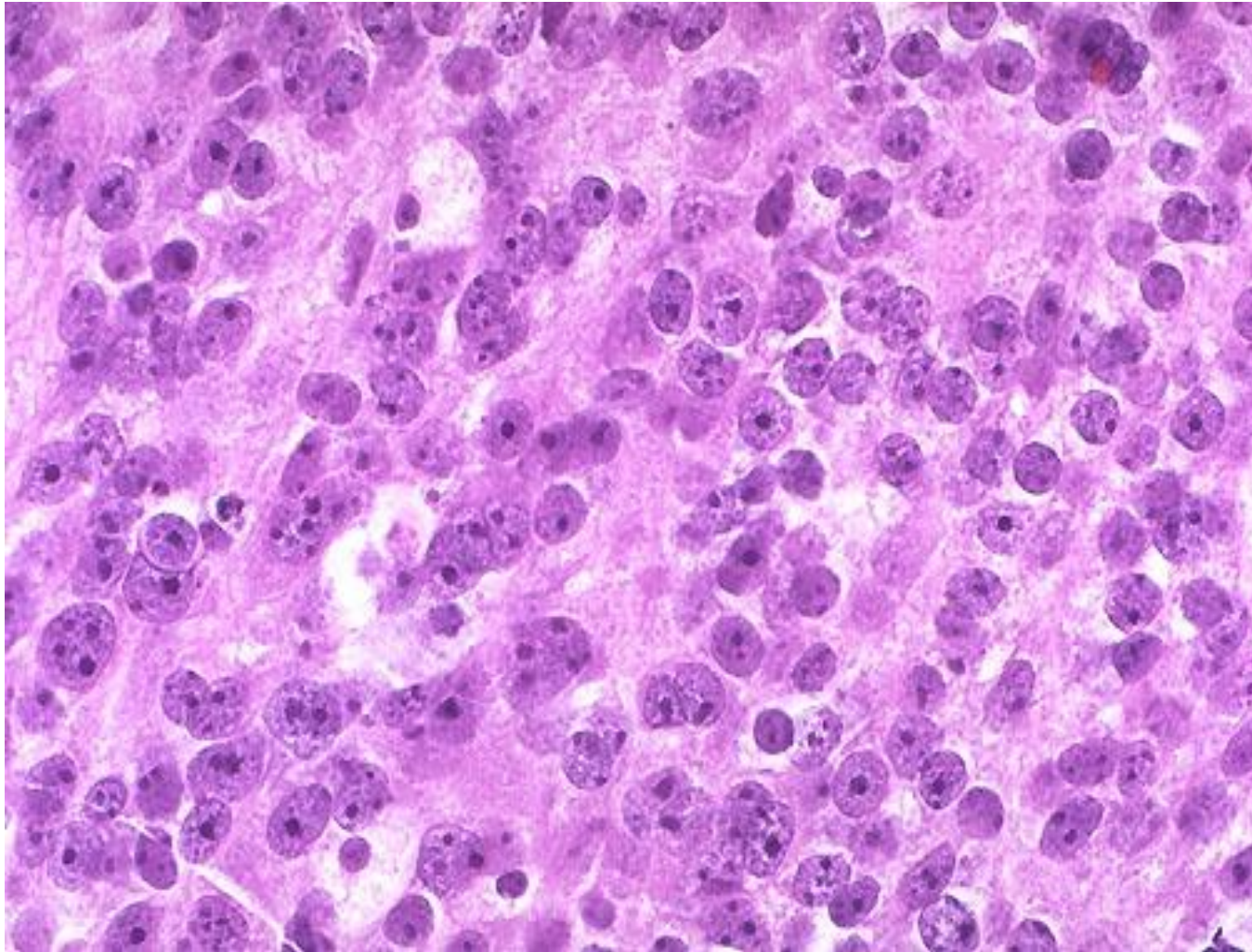




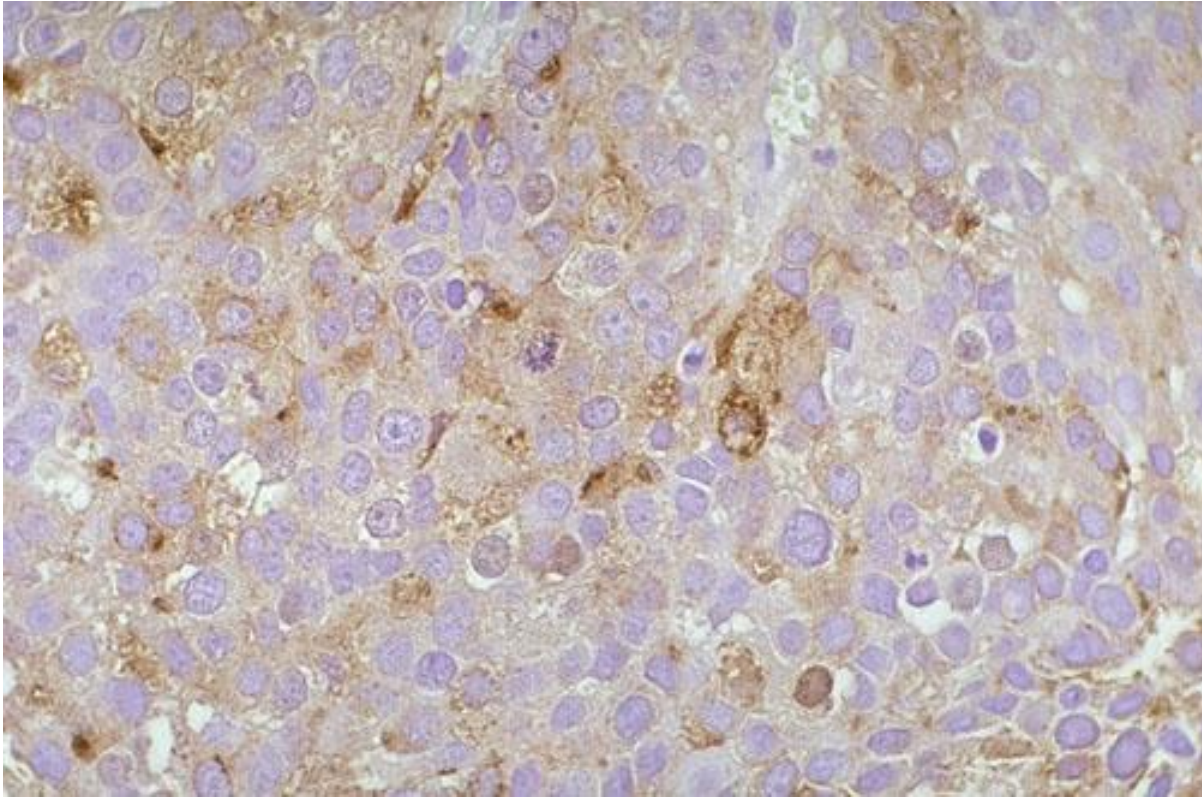
At the right are normal prostatic glands containing scattered corpora amylacea. At the left is prostatic adenocarcinoma. Note how the glands of the carcinoma are small and crowded.



At high magnification, the neoplastic glands of prostatic adenocarcinoma are still recognizable as glands, but there is **no intervening stroma**



Prominent nucleoli are seen in the nuclei of this prostatic adenocarcinoma, which is a characteristic feature.



Immunoperoxidase staining with antibody to prostate specific antigen (PSA).

PSA is also used as a serum test to monitor or detect prostate cancer.

Spread of Ca prostate

- **Local spread:** Tends to invade nerves, seminal vesicles & adjacent pelvic organs (local extension)
- **Lymphatic spread:** To para-aortic, iliac lymph nodes
- **Hematogenous metastases** : most often found in the vertebrae & sacrum; can also occur in kidneys, lungs & brain
- Bony metastases are often osteoblastic & are associated with elevated serum ***alkaline phosphatase***
- ***Visceral involvement occurs rarely***

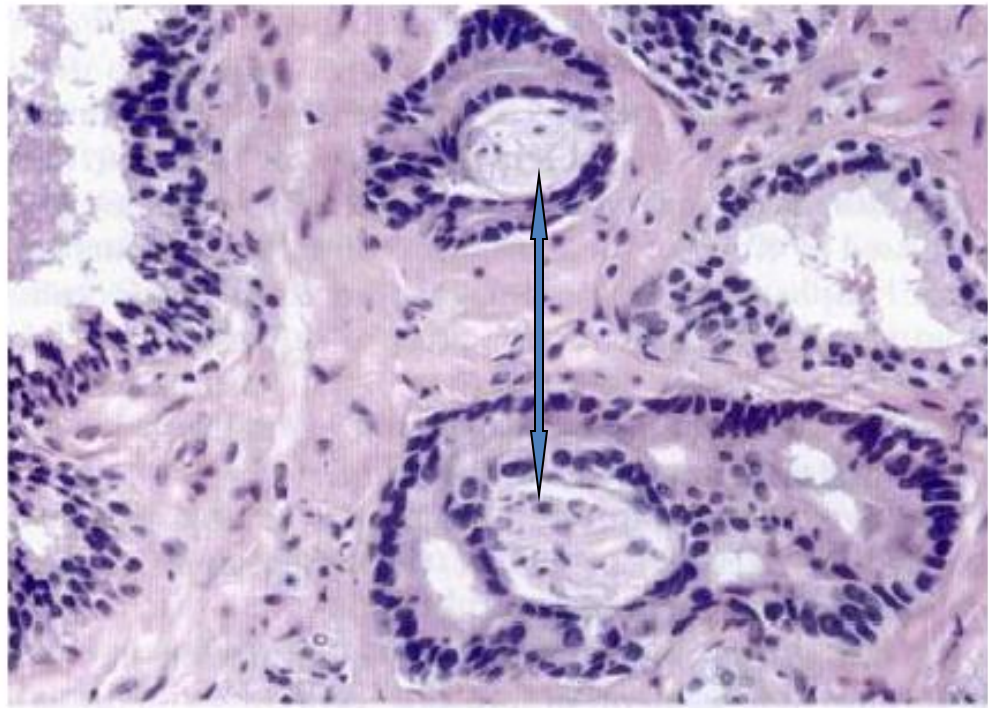


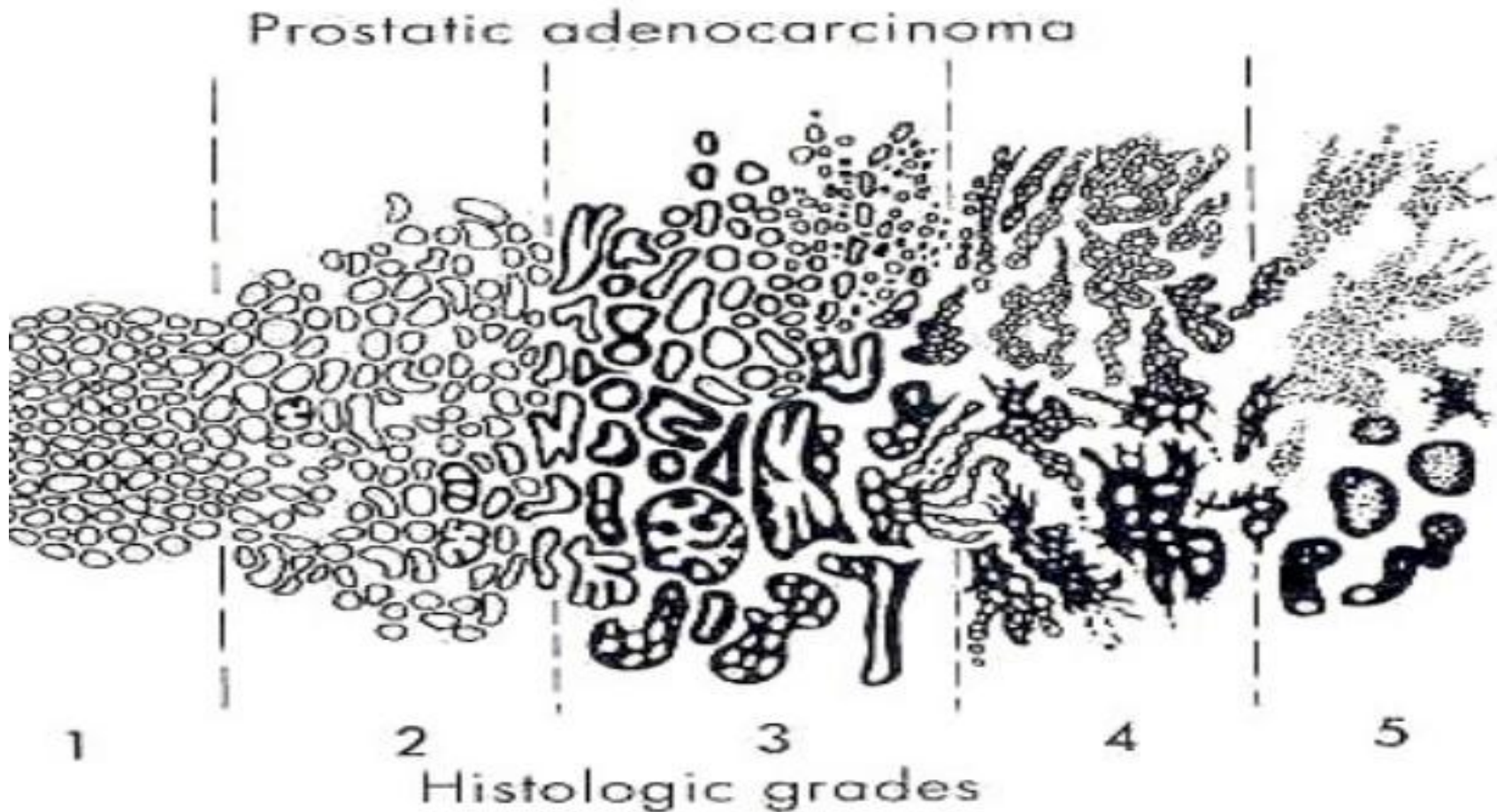
FIGURE 21-37 Carcinoma of the prostate showing perineural invasion by malignant glands. Compare to a benign gland (*left*).

FIGURE 21-35 Metastatic osteoblastic prostatic carcinoma within vertebral bodies.

Grading of prostatic carcinoma

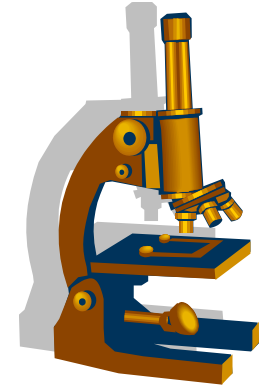
- The **Gleason system** is employed which stratifies prostate cancers into 5 grades based on the glandular patterns & degree of differentiation seen under low power magnification.
- **Grade 5** tumors show **least differentiation**
- Gleason score is based on Gleason grading : low-grade tumors have a relatively good prognosis & high-grade tumors are invariably lethal

Gleason Grading & Scoring of Prostatic Ca.



Diagnosis:

- Clinical: Digital Rectal examination (DRE)
 - hard, gritty, fixed tumor.
 - Loss of median groove.
- Imaging:
 - Ultrasonography (transrectal), CT Scan, MRI.
- Laboratory:
 - Tumor Marker – PSA
 - Biopsy - TURP
- Note: None of these methods can reliably detect small cancers & microscopic occult cancers may remain in-situ for several years. (PSA misleading*). Occult cancer is more common than clinical ca.



REFERENCE BOOK

- Robbins Basic Pathology : PAGE (663-668)

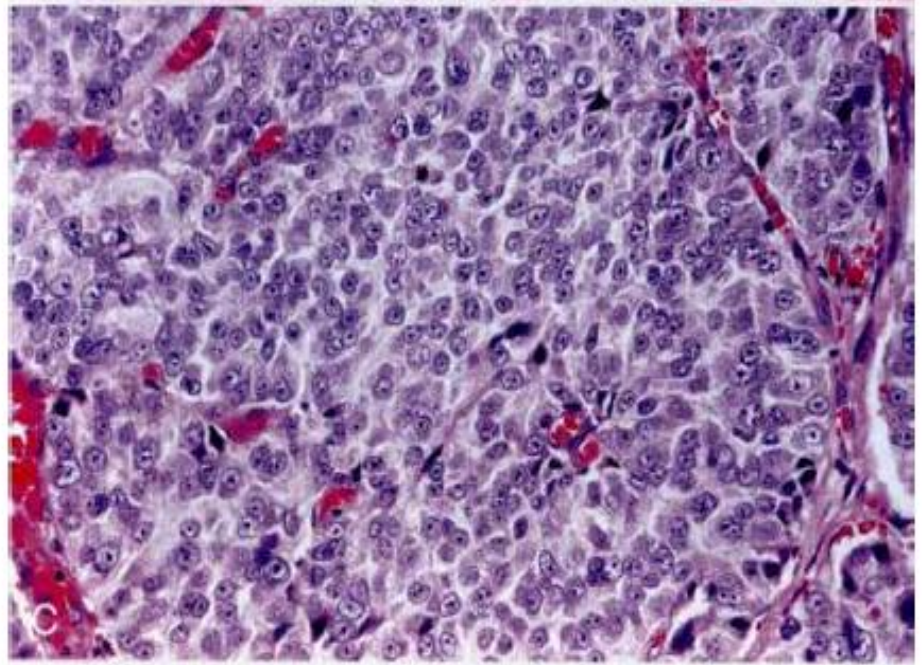
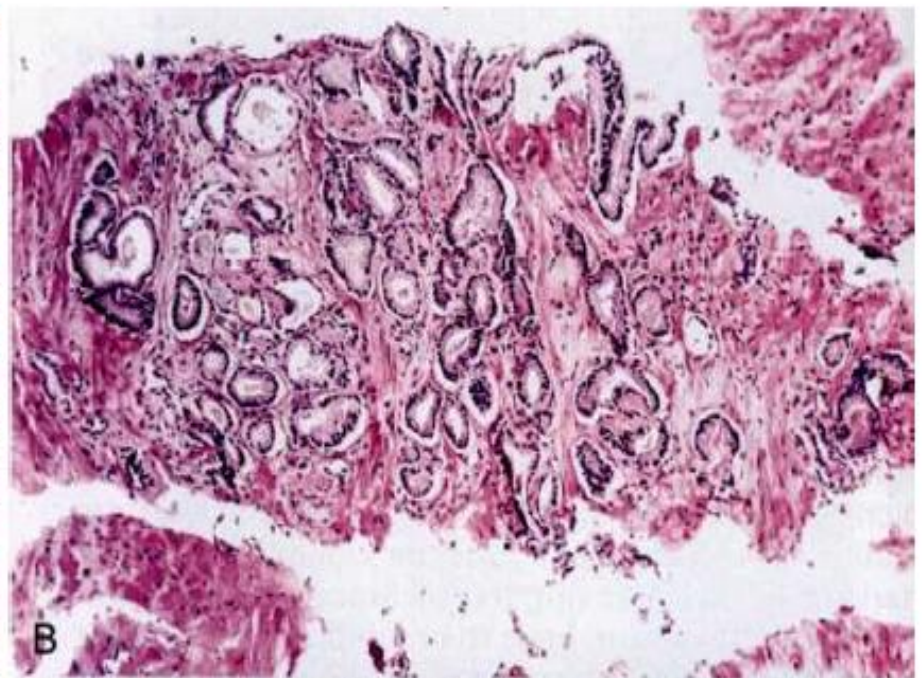
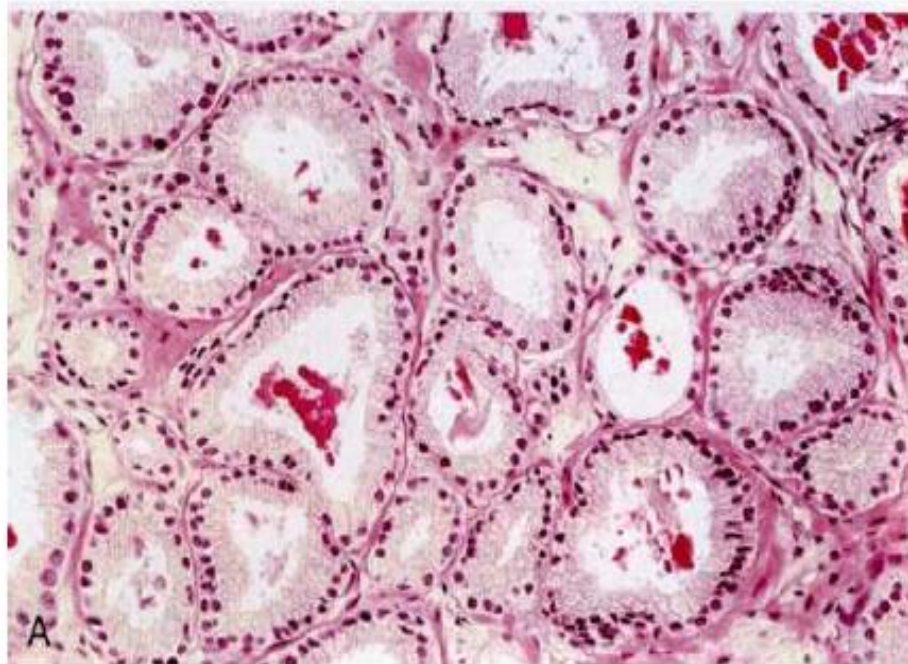


FIGURE 21-38 A, Low-grade (Gleason score $1 + 1 = 2$) prostate cancer consisting of back to back, uniformly sized malignant glands. Glands contain eosinophilic intraluminal prostatic crystalloids, a feature that is more commonly seen in cancer than in benign glands and more frequently seen in lower grade than in higher grade prostate cancer. B, Needle biopsy of the prostate with variably sized, more widely dispersed glands of moderately differentiated (Gleason score $3 + 3 = 6$) adenocarcinoma. C, Poorly differentiated Gleason score ($5 + 5 = 10$) adenocarcinoma composed of sheets of malignant cells.

Staging of carcinoma prostate: TNM

T1: Cancer found incidentally in TURP done for BPH

T2: Organ-confined cancer

T3a: Extraprostatic extension without seminal vesicle involvement

T3b: Extraprostatic extension with seminal vesicle involvement

T4: Direct invasion of contiguous organs

Prognosis of prostate carcinoma

- Localized low-grade tumors: 95% 10-year survival rate
- High-grade tumors extending to local tissues: 50% 5-year survival rate
- High-grade tumors with bone metastases or spread to distant sites: poor (2-3 year survival)